Radiosynoviorthesis in the Treatment of Disabling Arthritis

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Introduction

Chronic synovial inflammation leads to pannus formation and destruction of the articular cartilage. Synovitis results in proliferation of articular mucosa, destroys cartilage, penetrates bone, tears ligaments and tendons and results in joint destruction. Recurring hemarthrosis in hemophilia responds poorly to available therapy. Synovectomy is indicated in patients resistant to articular steroid injection. Chemical synovectomy using osmic acid or alkylating agents has limited acceptance. Surgical synovectomy is usually the treatment of choice and gives 2 to 3 years of relief. However, the long recovery period, expense, technical difficulty and post surgical complications, provide incentive to explore alternative forms of treatment like radionuclide synovectomy.

Radiosynoviorthesis means reconstruction/renewal of the articular mucosa (synovitis) with radioactive isotopes [1]. Radio nuclide synovectomy with radio colloidal gold (¹⁹⁸Au-colloid) has been used to alleviate pain and swelling of rheumatoid arthritis and related joint diseases for more than 40 years. Initial results were not encouraging due to non-availability of ideal radio pharmaceuticals but availability of ⁹⁰Y (Yttrium), ³²P (Phosphorus), ¹⁸⁶Re (Rhenium), ¹⁵³Sm (Samarium), ¹⁶⁵Dy (Dysprosium) and ¹⁶⁸Ho (Holmium) has given a fresh impetus.

The object of radio nuclide synovectomy is to destroy the diseased pannus and inflamed synovium by direct and selective irradiation with the expectation that the regenerated synovium will be free of disease. The histological changes include regression in size and hyperemia in the synovial villi, reduction of cellular infiltration and sclerosis of the synovium with minimal diffuse damage of articular cartilage.

Material and Methods

(a) Radiopharmaceuticals

An ideal radiopharmaceutical should have- Beta particle energy sufficient to penetrate and ablate the synovial tissue, but not severe enough to damage underlying articular cartilage or overlying skin, should be attachable to particles, small enough to be phagocytosed but large enough to remain within the joint cavity, should be biodegradable and have gamma emission, which will help in imaging. Ingrand suggested that the ideal particle size should be about 100 nm for uniform distribution and minimal lymphatic clearance [3]. The physical characteristics and recommended doses of radio pharmaceuticals commonly used in synovectomy are listed in Table 1.

(b) Radiation dosimetry

The radiopharmaceuticals listed in Table 1 deliver 6000 to 8000 rads to the synovium with a whole-body exposure of 0.4 rads [4]. Effective dose to the joints depend on - Size of the joint, Synovial thickness, Synovial structures (smooth, villous-fine/rough edematous), Condition of the joint fluid (watery or gelatinous) and Inflammatory activity of synovium.

(c) Methodology

Informed consent is obtained. Soft tissue scintigraphy is done using ^{99m}Tc MDP to visualize synovial inflammation and assess suitability. Ultrasonography of the joints is done. The procedure is carried under local anaesthesia and aseptic conditions. In large joint effusions synovial fluid is aspirated and 5-10 ml of saline is injected if there is no effusion. Radiotracer is injected into the joint, dose depending upon the radioisotope and the type of joint. Smaller joints require fluoroscopic guidance with contrast media to visualize joint space. Imaging is done under Gamma Camera to demonstrate the distribution of radiotracer in the joint cavity. Possible leakage is assessed using GM probe by sequential point counting over joints, regional lymph nodes and liver. Strict immobilization of the joint is ensured for at least 48 hours followed by gradual ambulation.

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Table 1**Characteristics of radiopharmaceuticals used for Radiosynovectomy**

Colloidal radio pharmaceuticals	Physical half life	Max energy and type	Range in tissues	Particle size	Dose	Remarks
Au-198	2.7 days	0.96Mev Beta, gamma	1.2-3.6mm	20-70um	7 mCi	Large joints
P-32 Chronic phosphate	14.3 days	1.7 Mev beta	2.6-7.9mm	0.6-4um	2 mCi	Large joints
Re-186	3.7 days	0.98 Mev beta, gamma	1.2-3.6mm	5-10 um	2.5mCi	Medium size joints
Y-90	2.7 days	2.2 Mev beta	3.6-11 mm	100 um	4 mCi	Large joints
Ho-166	1.1 days	1.84 Mev beta, gamma	1.9-5.7 mm	5-10 um	10mCi	Large joints
Dy-165 FHMA	0.1 days	1.29 Mev, beta, gamma	1.8-5.7mm	3-10nm	270 mCi	Large joints
Er-169	9.5 days	0,34 Mev beta	0.3-1mm	2-5um	1 mCi	Small joints

Indications and Contraindications**a) Indications:**

Indications include - Rheumatoid diseases, Vilonodular synovitis, Hemarthrosis/hemophilic joints and other arthrosis including osteoarthritis.

b) Contraindications:

Absolute contraindications are pregnancy and lactation.

Relative contraindications are children, adolescents, Peri articular sepsis and Unstable joint.

c) Complications

Complications are rare but include - General radiation reaction, Radiation synovitis, Tissue necrosis and Infection.

d) Questionable side effects

Questionable side effects include development of early degenerative joint, development of neoplasms and gene damage

Results

In 40-80% of cases pain, local hyperthermia and swelling decrease within 3-4 months. Approximately 75% of hemophilic joints have a decrease in the number of bleeding events. Grove et al in their series of 1500 patients of rheumatoid arthritis treated with 90Y reported excellent results (67%) and no untoward effects over several years of follow up. Kampen in his series reported 74% success rate in Rheumatoid arthritis and upto 50% in other arthritis. Patients with stage 1 disease (with no radiographic evidence of destructive changes) do best with 60% showing an excellent result with remission of pain and effusion. The greater the joint damage and thicker the synovium, the less satisfactory is the result.

Summary and conclusion

Localized irradiation of diseased synovium has been successfully done for over 4 decades. With development of newer radioisotopes, which are safer more than 75% patients have significant decrease in pain and swelling and in hemophilic joints reduction of bleeding episodes [5]. Kresnik et al carried out a meta analysis of 2190 joints treated during the period 1971-99 and shown overall response in $73 \pm 17\%$, $67 \pm 15\%$ of Rheumatoid arthritis, $52 \pm 24\%$ of osteoarthritis and $91 \pm 4\%$ of Hemophilic joints [6]. It is cost effective, safe and improves quality of life in patients with disabling arthritis [7]. The fear of developing cancer has been conclusively ruled out in extensive studies [8].

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